CLEAN SPECIFICATION
SERIAL NO. 09/125,841
PARAGRAPH AT PAGE 10, LINE 7 BRIDGING PAGE 11, LINE 12

D3

The expansion rates of $CD4^+$ cells present were comparable to the $CD8^+$ cells. In several model systems, the adoptive transfer of a mixed population of $CD4^+$ and $CD8^+$ cells has been more effective than purified $CD8^+$ cells, even when $CD8^+$ cells are central to desired response (Byrne, *et al.*, "Biology of Cloned Cytotoxic T Lymphocytes Specific for Lymphocyte choriomeningitis Virus: Clearance of Virus *in vivo*", *J. Virol.* 51:682-686, 1984; Larsen, *et al.*, "Role of T-Lymphocyte Subsets in Recovery from Herpes Simplex Virus Infection", *J. Virol.* ~~*Viol.*~~ 50:56-59, 1984; Lukacher, *et al.*, "*In Vivo* Effector Function of Influenza Virus-Specific T Lymphocyte Clones is Highly Specific", *J. Exp. Med.* 160:814-823, 1984). Although the infusion of $CD4^+$ cells, activated $CD4^+$ in particular, are the principal target for HIV-1 and critical to the progression of the infection, there are theoretical advantages to infusing $CD4^+$ cells along with $CD8^+$ cells. $CD8^+$ cells normally do not make enough IL-2 to support their own expansion and are dependent on IL-2, and possibly other cytokines from $CD4^+$ cells for "help". In the absence of T_H activity, an infusion of HIV-1-specific CTL would not be expected to expand *in vivo*. There also is evidence, at least in the case of influenza infections, that *ex vivo* expanded $CD4^+$ cells can mediate antiviral effects directly (Scherle, *et al.*, "Functional Analyses of Influenza-Specific Helper T Cell Clones *In Vivo*: T Cells Specific for Internal Viral Protein Provide Cognate Help for B Cell Responses to Hemagglutinin", *J. Exp. Med.* 164:1114-1121, 1986). There may be other advantages of using a mixed population of cells. Antibodies have been able to protect against experimental retroviral infections under some circumstances (Vaslin, *et al.*, "Induction of Humoral and Cellular Immunity to Simian Immunodeficiency Virus: What are the Requirements for Protection", *Vaccine* 12:1132-1140, 1994); correlative evidence suggests that some antibody may be associated with protection against progress of HIV-1 infection (Salk, "Prospects for the Control of AIDS by Immunizing Seropositive Individuals", *Nature* 327:473-476, 1987); long-term survivors of HIV-1 have been characterized by a strong neutralizing-antibody response (Pantaleo, *et al.*, "Studies in Subjects with Long-term Nonprogressive Human Immunodeficiency Virus Infection", *N. Eng. J. Med.* 332:209-216, 1995, Cao, *et al.*, "Virologic and Immunologic Characterization of Long-Term Survivors of Human Immunodeficiency Virus Type 1 Infection", *N. Engl. J. Med.* 332:201-208, 1995); and the infusion of plasma rich in anti-HIV-1 antibody has been reported to delay the appearance of the first AIDS-defining event (Vittecoq, *et al.*, "Passive Immunotherapy in AIDS: A Double-Blind Randomized

Study Based on Transfusions of Plasma Rich in Anti-Human Immunodeficiency Virus 1 Antibodies *vs.* Transfusion of Seronegative Plasma, *Proc. Natl. Acad. Sci. USA*, 92:1195-1199, 1995). $CD8^+$ T_H cells are well-recognized. Thus, there is a potential advantage to the infusion of cells that can provide T_H activity to B-cells. Some of the $CD8^+$ cells were also $CD45RA^+$ or $CD30^+$, suggesting the possibility of $CD8^+$ T_H function *in vivo*, including the induction of anti-HIV-1 antibody (Manetti, *et al.*, *supra*). The release of T_H1 cytokines, such as IFNg, suggests the possibility that DTH responses can be enhanced. The study of Carter, *et al.*, (*supra*) has suggested the feasibility and safety of infusing a mixed population of uninfected $CD4^+$ and $CD8^+$ cells into HIV-1-infected individuals.